

WHAT IS CLAIMED IS:

1. A method of inducing tolerance to a transplant transplanted from a donor to a recipient, the method comprising:

- (a) culturing an HPC population under growth conditions suitable for inducing or enhancing veto activity in at least a portion of said HPC population, thereby generating a tolerance-inducing cell population; and
- (b) administering a dose of said tolerance-inducing cell population prior to, concomitantly with or following transplantation of the transplant, thereby inducing tolerance to the transplant in the recipient.

2. The method of claim 1, further comprising the step of conditioning the recipient under sublethal, lethal or supralethal conditions prior to step (b).

3. The method of claim 1, wherein the donor is selected from the group consisting of an allogeneic donor and a xenogeneic donor.

4. The method of claim 1, wherein the donor and the recipient are both humans.

5. The method of claim 1, wherein the transplant is selected from the group consisting of cells, a tissue and an organ.

6. The method of claim 1, wherein said growth conditions are selected so as to induce myeloid differentiation in said HPC population.

7. The method of claim 1, wherein said growth conditions are selected so as to induce differentiation into CD33⁺ cells in said HPC population.

8. The method of claim 1, wherein said tolerance-inducing cell population predominantly displays a characteristic associated with a myeloid phenotype.

9. The method of claim 1, wherein said tolerance-inducing cell population predominantly expresses CD33.

10. The method of claim 1, wherein said veto activity is enhanced per cell in said HPC population.

11. The method of claim 1, wherein said dose of tolerance-inducing cells possesses sufficient veto activity so as to enable engraftment of MHC-mismatched transplants.

12. A method of transplanting a transplant derived from a donor to a recipient, the method comprising:

- (a) administering to the recipient a dose of cultured HPCs, said cultured HPCs having enhanced veto activity as compared to non-cultured HPCs; and
- (b) transplanting the transplant to the recipient.

13. The method of claim 12, further comprising the step of conditioning the recipient under sublethal, lethal or supralethal conditions prior to step (b).

14. The method of claim 12, wherein step (a) is performed prior to, concomitantly with or following step (b).
15. The method of claim 12, wherein the donor and the recipient are both humans.
16. The method of claim 12, wherein the transplant is selected from the group consisting of cells, a tissue and an organ.
17. The method of claim 12, wherein said cultured HPCs are cultured *in vitro*.
18. The method of claim 12, wherein said cultured HPCs predominantly display a characteristic associated with a myeloid phenotype.
19. The method of claim 12, wherein said cultured HPCs predominantly express CD33.

20. The method of claim 12, wherein said enhanced veto activity is enhanced per cell in said cultured HPCs.

21. The method of claim 12, wherein said dose of cultured HPCs possesses sufficient veto activity so as to enable engraftment of MHC-mismatched transplants.

22. A method of predicting the veto activity of a population of cultured HPCs, the method comprising:

- (a) identifying cells displaying a characteristic associated with a myeloid phenotype in the population of cultured HPCs; and
- (b) determining within the population of cultured HPCs a ratio between cells displaying said characteristic associated with a myeloid phenotype and cells not displaying said characteristic associated with a myeloid phenotype.

23. The method of claim 22, wherein said step of identifying cells displaying a characteristic associated with a myeloid phenotype in the population of cultured HPCs is effected by detecting cells expressing a

myeloid-specific molecule selected from the group consisting of an intracellular protein, a membrane-bound protein, a secreted protein, a messenger RNA (mRNA) transcript, a lipid, a carbohydrate, a hormone and a metabolite.

24. The method of claim 22, wherein said characteristic associated with a myeloid phenotype in the population of cultured HPCs is expression of CD33.

25. The method of claim 22, wherein said step of identifying cells displaying a characteristic associated with a myeloid phenotype in said population of cultured HPCs is effected by a method selected from the group consisting of antibody recognition, ligand recognition and polymerase chain reaction (PCR) amplification.

26. The method of claim 22, wherein said step of identifying cells displaying a characteristic associated with a myeloid phenotype in said population of cultured HPCs is effected by detection of a physical criterion, said physical criterion selected from the group consisting of cellular

morphology, cell size, cell density, cellular organelle morphology, cellular organelle size and cytoplasmic light scattering.

27. The method of claim 22, wherein said step of identifying cells displaying a characteristic associated with a myeloid phenotype in the population of cultured HPCs is effected by histological staining or by a functional cellular or biochemical assay.

28. The method of claim 22, further comprising the step of correlating the veto activity of the population of cultured HPCs with said ratio.

29. A method of isolating cells possessing veto activity from a population of cultured HPCs, the method comprising:

- (a) contacting the population of cultured HPCs with a composition-of-matter capable of specifically binding to a cell displaying a characteristic associated with a myeloid phenotype; and

- (b) isolating said cells specifically contacting said composition-of-matter.

30. The method of claim 29, wherein said composition-of-matter includes a binding moiety selected from the group consisting of an antibody, a T cell receptor, a biological ligand and a synthetic ligand.

31. The method of claim 29, wherein said composition-of-matter further includes a supporting matrix, whereas said binding moiety is attached to said supporting matrix.

32. The method of claim 29, wherein said composition-of-matter specifically binds to a molecule selected from the group consisting of a protein, a lipid and a carbohydrate.

33. The method of claim 29, wherein said composition-of-matter specifically binds to a cell displaying CD33.

34. A method of treating or preventing an autoimmune disease in a subject, the method comprising administering to the subject a therapeutically effective amount of HPCs displaying at least one antigenic determinant associated with the autoimmune disease to thereby at least partially prevent or alleviate the autoimmune disease in the subject.

35. The method of claim 34, further comprising generating said HPCs displaying at least one antigenic determinant prior to said administering.

36. The method of claim 35, wherein said generating is effected by pulsing a population of HPCs with a molecule including said at least one antigenic determinant.

37. The method of claim 35, wherein said generating is effected by transforming a population of HPCs with at least one polynucleotide encoding said at least one antigenic determinant.

38. The method of claim 37, wherein said population of HPCs is allogeneic with respect to the subject and whereas said at least one polynucleotide further encodes an MHC molecule which is syngeneic with respect to the subject.

39. The method of claim 35, further comprising culturing said HPCs prior to, concomitantly with or following said generating.

40. The method of claim 39, wherein said culturing is effected under conditions suitable for the formation of a myeloid phenotype in at least a portion of said HPCs.

41. The method of claim 34, wherein said at least one antigenic determinant associated with the autoimmune disease is derived from a polypeptide selected from the group comprising myelin basic protein, insulin, glutamic acid decarboxylase and collagen.

42. A population of cells comprising HPCs displaying at least one antigenic determinant associated with an autoimmune disease.

43. The population of cells of claim 42, wherein said HPCs are cultured HPCs predominantly displaying a characteristic associated with a myeloid phenotype.

44. The population of cells of claim 42, wherein said HPCs displaying at least one antigenic determinant are generated by pulsing said HPCs with a peptide including said at least one antigenic determinant.

45. The population of cells of claim 42, wherein said HPCs displaying at least one antigenic determinant are generated by transforming a said HPCs with a polynucleotide encoding said at least one antigenic determinant.

2001 JUN 18 18:54